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Original Research Article

Study of Inflammatory Markers and Lipid Profiles on Obese and Non-Obese Patients with Rheumatoid Arthritis

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Abstract

Obesity has been identified as a significant risk factor for various chronic diseases, including rheumatoid arthritis (RA), which is characterized by joint inflammation. Obesity is also associated with increased levels of inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). The objective of this study was to examine whether obesity has a confounding effect on ESR and CRP levels in patients with RA who are in a low disease activity state or remission, as indicated by the clinical disease activity index (CDAI).

Material and Methods: To categorize adult rheumatoid arthritis (RA) patients based on body mass index, the study divided them into two groups: obese and non-obese. Additionally, relevant exclusions were implemented to eliminate factors that could contribute to elevated inflammatory markers. The study then conducted an analysis comparing C-reactive protein (CRP), lipid profile, and erythrocyte sedimentation rate (ESR) differences between the obese and non-obese groups.

Results: In comparison to non-obese individuals (n = 28), obese patients with RA (n = 28) exhibited higher CRP and ESR (p-values 0.0001 and 0.001, respectively). Additionally, compared to non-obese females, obese females with RA had significantly higher CRP and ESR levels. In contrast, men did not significantly differ. Two non-obese RA patients (3%), and twenty-one obese (24.7%) RA patients, both showed increased CRP (difference of about 22% [24.7 minus 3]. The difference between 16 non-obese and 40 obese RA patients with high ESR was almost 23% (47 minus 24.2).

Conclusion; Therefore, we conclude that 22% and 23% of patients, respectively, obesity was the attributable cause of falsely elevated CRP and ESR.

Keywords: Rheumatoid arthritis, C-reactive protein, ESR, Lipid profile.

Introduction

Rheumatoid arthritis (RA) and other autoimmune and inflammatory illnesses are significantly influenced by obesity. Increased body mass index (BMI) has been shown to

paradoxically correlate with disease activity [1]. The level of disease activity is determined in large part by acute phase reactants (APR) [2]. In rheumatoid arthritis (RA), a chronic systemic inflammatory disorder, elevated levels of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are indicative of active disease and can be used as biomarkers to monitor disease activity.

Acute phase reactants are also used to monitor RA patients and gauge how well their treatments are working. Studies have demonstrated that elevated CRP and ESR in the general population are strongly linked with obesity [3,4].

Infection and inflammation also cause an increase in acute phase reactants. They are crucial parts of numerous composite indices used to gauge the severity of the RA disease. Independent of the severity of the disease, obesity can cause RA patients' acute phase reactants to artificially increase [3]. This might result in erroneously high results for a variety of disease activity assessments that include acute phase reactants, making it challenging to accurately quantify disease activity.[5-8]

The primary aim of the study was to assess the frequency at which obesity has a confounding effect on C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) levels in rheumatoid arthritis (RA) patients who are in remission or a low disease activity state, using the clinical disease activity index (CDAI). Additionally, the study aimed to investigate the impact of gender on CRP and ESR levels in RA patients. Overall, the study sought to determine the extent to which elevated levels of inflammatory markers in RA patients are attributable to obesity.

Material and Methods

This study comprised a total of 56 participants with a RA diagnosis. They were split into two groups of equal age, gender, BMI (based on WHO BMI measurements), and co morbidities, with 28 obese patients and 28 non-obese patients in each group. The levels of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were examined, and the Disease Activity Score 28-joint C-reactive protein (DAS28-CRP) and ESR were used to calculate the activity level. Serum samples were taken in order to obtain lipid profiles.

In order to ensure the study results were not confounded by other inflammatory disorders or medical conditions, patients with a recent major surgery within the past three months, pregnancy, anaemia (haemoglobin < 10 g/dl), current smoking, polycythaemia, sickle cell anaemia, liver disease, malignancy, or overlap with another connective tissue disease such as interstitial lung disease, chronic obstructive pulmonary disease, scleritis/episcleritis, or rheumatoid vasculitis, were excluded from the study.

Results

Twenty-eight obese patients with RA (16 males [M], 12 females [F]), 28 non-obese RA patients (17 M, 11F), were recruited into the study (Table I).

Table 1: Baseline characteristics

Parameters	Obese RA (*n* = 28)	Non-obese RA (*n* = 28)
Number of males (%)	16(4.48)	17 (4.76)
Number of females (%)	12 (3.36)	11 (3.30)
Mean disease duration (months)	114.75	76.9

Mean BMI (kg/m^2)	27.5	25.6
Median CDAI (IQR)	1.33 (5)	1.43 (4)
Mean CDAI (SD)	2.53 (3.16)	2.07 (2.8)
Median CRP (IQR)	5 (5.7)	3 (3)
Median ESR (IQR)	30 (21)	18 (19.5)
Mean CRP (SD)	9.9 (13.01)	4.7 (7.96)
Mean ESR (SD)	30.7 (17.13)	20.4 (13.01)

RA – rheumatoid arthritis, BMI – body mass index, CDAI – clinical disease activity index, IQR – interquartile range, CRP – C-reactive protein, ESR – erythrocyte sedimentation rate, SD – standard deviation.

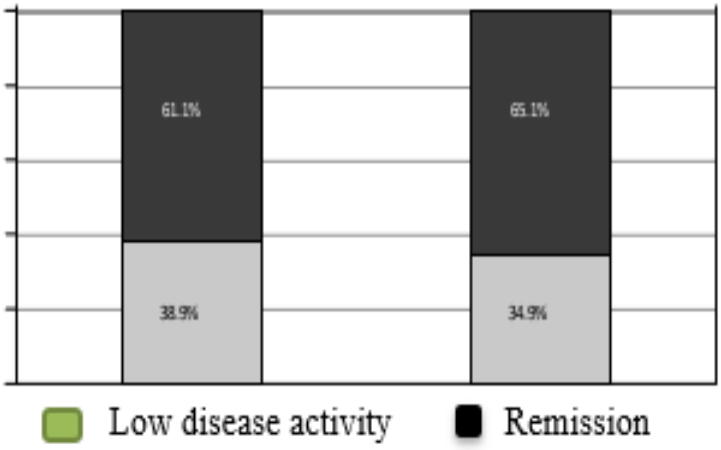

Figure 1: Disease activity state in patients with rheumatoid arthritis (RA)

Obese patients had significantly higher CRP and ESR than non-obese patients (*p*-values 0.008 [effect size 0.2984] and 0.000005 [effect size 0.3466], respectively) . Obese RA patients' CRP levels were not significantly different from those of obese controls (p-value [effect size 0.283]). For men (p-value 0.964 [effect size 0.0815] and 0.051 [effect size 0.2841], respectively), the difference in CRP and ESR between obese and non-obese RA patients was not statistically significant, in contrast to women (p-value 0.008 [effect size 0.324] and 0.0001 [effect size 0.34], respectively). Between the two groups, there were no appreciable differences in CRP levels between the genders. Both obese and non-obese RA patients had similar ESR values. In contrast, the difference in ESR between the obese control group's male and female participants has just recently attained statistical significance (median 21.5 and 16, respectively; p-value 0.048 [effect size 0.2384]).

CRP values were higher than 10 mg/l in two obese RA patients (24.7%) and two non-obese RA patients (3%); this represents a difference of almost 22% between the two groups (24.7% minus 3). In a similar vein, 16 non-obese RA patients and 40 obese RA patients (a difference of approximately 23% [47 minus 24.2]) both exhibited ESR levels greater than 30 mm/hr. Therefore, obesity caused falsely elevated CRP and ESR in 22% and 23%, respectively, of RA patients.

Table 2: Lipids and Metabolic Profile

S.No	Variables	Obese (N=28) Mean ± SD	Non- obese(n=28) Mean ± SD	P – Value
1	Total Cholesterol (mg/dL)	169.2 ± 72.7	113 ± 37.6	0.008
2	LDL-C (mg/dL)	155.5 ± 39 .7	132.7 ± 37.5	Ns
3	HDL-C (mg/dL)	72.5 ± 18.5	61.4± 22.6	Ns
4	ApoA1 (g/L)	1.9 ± 0.27	1.76 ± 0.47	Ns
5	ApoB (g/L)	1.4 ± 0.21	1.0 ± 1.4	Ns
6	FG (mg/dL)	90.9 ± 14.2	81.3 ± 11.5	0.01
7	Insulin, (µ/mL)	16.4 ± 6.3	8.7 ± 3.8	0.0001
8	HOMA-I	3.3 ± 0.61	1.6 ± 0.81	<0.0001
9	25(OH)D (ng/mL)	6.6 ± 2.4	10.8 ± 6.7	0.01

The metabolic indices serum TG ($p = 0.008$), fasting glucose ($p = 0.01$), and insulin concentrations ($p = 0.0001$) were also considerably higher in RA obese patients. Additionally, their DAS28-CRP ($p = 0.04$) and HOMA-I (p 0.001) results were significantly better. As opposed to the RA MetS patients, these individuals had lower serum [25(OH)D] concentrations ($p = 0.01$) (Figure 1). But between the two RA subgroups, there were no statistically significant differences in the serum levels of HDL-C ($p = 0.70$), LDL-C ($p = 0.10$), Apo-A ($p = 0.12$), or Apo-B ($p = 0.14$).

Discussion

The findings from our study indicate that obese patients with rheumatoid arthritis (RA) exhibited significantly elevated levels of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) compared to non-obese RA patients. Interestingly, there was no noticeable distinction in CRP levels between obese RA patients in a state of low disease activity/remission and obese individuals without RA. These results suggest that obesity is the primary factor contributing to the heightened CRP levels in this context. Within our sample of male individuals diagnosed with rheumatoid arthritis (RA), we observed that obesity did not show a significant association with elevated levels of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). These findings align with a study conducted by George *et al*., which reported similar results. (8) A notable study conducted by George *et al*. revealed a positive correlation between C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) with obesity specifically in females diagnosed with rheumatoid arthritis (RA), while no significant association was observed in males. This comprehensive study examined the relationship between CRP, ESR, and obesity in two separate cohorts of individuals with RA, as well as a control cohort without RA. Dual-energy X-ray absorptiometry (DEXA) was utilized to assess truncal fat levels. Interestingly, both females with RA and those without RA exhibited a positive link between CRP and body mass index (BMI). Among females, a similar relationship was observed between erythrocyte sedimentation rate (ESR) and body mass index (BMI). However, when fat mass was considered as a variable, the correlation between C-reactive protein (CRP) and BMI vanished, indicating that fat mass played a crucial role in the association between CRP and BMI. Adipose tissue serves as a significant source of various mediators of inflammation, such as interleukin 6 (IL-6), which are involved in the inflammatory processes. [9]. The increase in acute phase reactants observed in obese individuals is believed to be a consequence of the heightened inflammatory

state associated with excess adipose tissue. In the case of men with rheumatoid arthritis (RA), George *et al*. hypothesized that the weak association between C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) with body mass index (BMI) could be attributed to weight loss resulting from inflammation due to active disease.

Smaller studies have shown correlations between fat mass and CRP in women with RA (10–12), most notably a study by Giles *et al*. using the ESCAPE-RA cohort (one of three studies included in the BC cohort). The current study is the largest to address this issue and shows how inflammatory markers affect different BMI categories. Although BMI is a clinically available but imperfect measure of adiposity, especially in RA, this study also shows that it is strongly associated with inflammatory markers in women with RA.

According to our research, TG, LDL cholesterol, systolic and diastolic blood pressure, and serum 25-(OH)D levels are all related to BMI. The existence of MS and its components, such as blood pressure and TG, were also strongly inversely correlated with serum 25-(OH)D levels, as we also found. After taking into consideration potential confounding factors, the results were still significant. Previous research found erratic relationships between 25-(OH)D levels and MS and its elements.

The 25-(OH) D level is inversely correlated with MS in Western populations, according to several epidemiologic research [13-16]. In the clinical investigation, those with low levels of vitamin D were approximately three times more likely to have MS than those with normal levels [17]. Asian populations [18] also have similar verse-verse relationships. On the other hand, several investigations [19-20] were unable to demonstrate a link between a 25-(OH) D shortage and the occurrence of MS. Additionally, by controlling extracellular calcium levels, which are necessary for insulin-mediated intracellular processes, it indirectly influences insulin sensitivity in skeletal muscle and fat tissue [21]. Vitamin D deficiency increases the likelihood of developing insulin resistance, which may lead to an increase in TG and VLDL levels and is related to insulin sensitivity [22].

Conclusion

The results of our study suggest that obese individuals with rheumatoid arthritis (RA) may benefit from increased frequency of follow-up appointments in order to effectively manage disease activity. Moreover, it is crucial to pay close attention to lipid profile management in these patients, while considering the inclusion of vitamin D supplementation. This approach not only promotes bone health but also has the potential to alleviate the inflammatory repercussions arising from involvement of both joint and adipose tissue.

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